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Effect of Certain Nutritional Deficiencies on Various Phosphorus-containing Fractions of the Chick Brain.*

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In a series of studies designed to investigate the lipids of the brain in nutritional deficiencies it became apparent that a metabolic disturbance occurred which resulted in a variation in the phosphorus distribution. The early work dealt mainly with tissues from animals suffering from deficiencies of the B complex. The work of Sure and Buchanan[1] had indicated that a disturbance of the blood serum phosphatase occurred in the vitamin B complex deficiencies. It seemed worth while to make a more extensive study of the brain phosphorus of chicks on diets low in certain essential factors.

The nutritional deficiencies were produced in our laboratory in collaboration with Elvehjem and associates. The following deficiency conditions were studied: vitamin A, vitamin B_4, and encephalomalacia. Chicks of the same age, on a ration known to be adequate in all these factors, were sacrificed as controls. The chicks with typical deficiency symptoms were killed at the age of 10-21 days by bleeding through the carotid artery. The brains were immediately removed and sliced mid-sagitally; half of the brain was preserved for histologic study, the other half was placed in a drying oven at 56°-58°C. for 48 hours.

The method of extraction of the dried brains was essentially that of Bloor,[2] using hot ethyl alcohol and repeated extractions. The brains were ground, extracted repeatedly with hot alcohol and the extracts were decanted and made up to volume in 100 cc. flasks. No inorganic phosphorus was detected in the extracts, therefore only the total phosphorus was determined on suitable aliquots. The brain residue was dried and weighed. The phosphorus was partitioned according to the principle described by Hawk and Bergeim[3] and determined by the method of Fiske and Subbarow.[4] The residue after alcoholic extraction was extracted with trichloracetic acid.

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1 Sure, B., and Buchanan, K. S., *Am. J. Digest. Dis. and Nutr.*, 1936, **3**, 493.

2 Bloor, W. R., *J. B. C.*, 1929, **82**, 273.

3 Hawk and Bergeim, *Practical Physiological Chemistry*, 11 ed., 1937, 460.

4 Fiske, C. H., and Subbarow, Y., *J. B. C.*, 1925, **66**, 375.

TABLE I.
Phosphorus Content of Chick Brain.

Disease	Total No. of chicks used	Total acid-soluble P in Ccl_3COOH extract (mg. %)		Inorganic P in Ccl_3COOH extract (mg. %)		Ester P in Ccl_3COOH extract (mg. %)		% alcohol extract		P in alcohol extract (mg. %)	
		Range	Ave.	Range	Ave.	Range	Ave.	Range	Ave.	Range	Ave.
Controls	31	3.6-6.6	4.9	2.4-3.7	3.0	0.3-3.7	2.0	39.3-51.4	47.6	2.4-10.5	6.3
A-deficient	24	3.1-7.2	4.8	3.0-4.6	3.7	trace-3.2	1.0	42.3-54.0	47.8	4.0-14.1	8.1
B_4 "	29	3.1-6.2	4.3	2.3-4.4	3.5	trace-2.2	0.8	43.6-57.0	47.5	3.3-12.1	7.6
Encephalomalacia	24	3.0-6.4	4.5	2.8-4.9	3.5	trace-3.0	1.0	44.6-53.2	48.8	3.5-11.0	7.2

Inorganic phosphorus and total acid soluble phosphorus were determined on suitable aliquots of this extract and the difference between the two was used as a measure of the ester phosphorus. The residue remaining after alcoholic and trichloracetic acid extractions was digested (wet ash) and the total phosphorus determined.

Table I contains the condensed results of these studies. Inspection of the table indicates that the ester phosphorus was considerably reduced in the nutritional deficiencies. The greatest reduction occurred in vitamin B_4 deficiency. It was also noted that the inorganic phosphorus was increased, but the increase was not equal to the amount of reduction in the ester phosphorus. Consequently, the total acid soluble phosphorus was lowered.

The phosphorus content of the alcoholic extract was slightly increased in the deficiency diseases as compared to the values observed in the controls. The phosphorus in the residue of the brain after alcoholic and trichloracetic acid extraction was apparently unaffected and contained from 1.2-1.3 mg. % for all groups. No difference was noted in the quantity of the alcohol-soluble fraction of the normal chick brain as compared to the deficient brains. The total phosphorus content of the brain of the deficient chicks was, however, equal to that of the control chicks and contained from 12.1 to 13.1 mg. %. Thus it appears that a vitamin A deficiency, encephalomalacia, or B_4 deficiency causes a disturbance in the phosphorus distribution in the chick brain.

The reduction in ester phosphorus in the brains of the nutritional deficiencies studied appears to be of importance. In 35% of the cases the amount of ester phosphorus calculated to be present in vitamin A or B_4 deficiency, or in encephalomalacia was *nil* or exceedingly low. Coincident with the lowering of ester phosphorus was an increased inorganic phosphorus. These findings indicate a disturbance in phosphorus metabolism. It is possible that phosphorylation does not occur, or if so, it proceeds at a greatly reduced rate, or dephosphorylation occurs at an excessive rate.

Summary and Conclusions. The various fractions of chick brain, namely, the alcohol extract fraction, the trichloracetic acid extract fraction, and the fraction remaining after both extractions, were analyzed for their phosphorus content. In comparing the values obtained from chicks on a normal ration with those obtained from chicks receiving rations low in one of the essential factors (vitamin A, vitamin B_4, and encephalomalacia) the following results were obtained.

The ester phosphorus of the trichloracetic acid fraction was mark-

edly reduced in the deficiency diseases, while the inorganic phosphorus was increased but not to the same extent as the former was reduced. The alcohol extract phosphorus fraction was only slightly increased. The phosphorus of the brain residue after alcohol and trichloracetic acid extractions as well as the total phosphorus content of brain was unaffected. Further, the amount of alcohol-soluble material of the brains was similar in both deficient and control chicks. Certain nutritional deficiencies, among them the lack of the encephalomalacia factor, vitamin A, or B_4, cause a disturbance of normal phosphorus metabolism in the brain of the chick.

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Relation of the Carrier State to Pneumococcal Peritonitis in Young Children with the Nephrotic Syndrome.

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Most deaths in children afflicted with the nephrotic syndrome are caused by intercurrent infection. In nearly every instance, the infection is due to the pneumococcus, and the site of localization is the peritoneal cavity.

In the nephrotic child peritonitis develops suddenly, and without any apparent precipitating factor such as an upper respiratory infection. This fact suggests two possibilities: First, that peritonitis is due to the acquisition from a carrier of an invasive strain of pneumococcus, and second, that peritonitis is caused by the strain or strains of pneumococcus which are carried in the patient's nasopharynx.

Nose and throat cultures have been made periodically on 12 nephrotic children, 1½ to 7 years of age. The children have been observed over periods varying from one week to 2 years. The pneumococci isolated from the nasopharynx have been typed by Neufeld's technic. Only those studies are presented here which deal with the children developing peritonitis.

In every child who developed peritonitis, the same type of pneumococcus has been recovered from the throat and the peritoneal cavity. During the carrier-state repeated cultures showed the same type or types of pneumococcus to persist in the nasopharynx. In 2